Type: Poster Presentation

Final Abstract Number: 40.030
Session: Virology and Viral Infections (Non-HIV)
Date: Thursday, June 14, 2012
Time: 12:45-14:15
Room: Poster & Exhibition Area

The effect of andrographolide on Human papillomavirus type 16 (HPV16) positive cervical cancer cells (SiHa)

S. Fangkham[1,*], T. Ekalaksananan[1], C. Aromdee[2], S. Seubsasana[3], B. Kongyingyoes[4], N. Patarapadungkit[5], C. Pientong[1]

[1] *Department of Microbiology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand*
[2] *Pharmaceutical Chemistry, Faculty of Pharmaceutical Sciences, Khon Kaen University, Khon Kaen, Thailand*
[3] *Department of Medical Sciences, Ministry of Public Health, Regional Medical Science Center Ubon Rajathanee, Ubon rajathanee, Thailand*
[4] *Department of Pharmacology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand*
[5] *Department of Pathology, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand*

Background: Infection with a high-risk human papillomavirus (HR-HPV), especially, HPV16 is the most important risk factor for cervical cancer. Oncoproteins (E6 and E7) of HR-HPV play an important role in cervical cancer development involved by several mechanisms including degradation of tumor suppressor protein p53 and anti-apoptosis. Andrographolide is a diterpenoid lactone isolated from a traditional herbal medicine,Andrographis paniculata. It has been reported to induce apoptosis in different cancer cell lines. However, the effects on regulation of HPV16 transcription, oncogene expression and induction of cervical cancer cells apoptosis are still unclear. This study investigated the effects of andrographolide on HPV16 transcription activity, E6 oncogene expression and p53 protein level as a downstream process involved in cell apoptosis.

Methods: Sub-cytotoxicity of the andrographolide compound was determined by MTT assay. C33A cell line, an HPV- negative cervical cancer cell line, was transfected by reporting vector containing long control region of HPV16 European and Asian variant and treated with compound for analysis of promoter transcription. SiHa cell line, an HPV16-positive cervical cancer cell line, was treated with the compound for 24 and 48 hr. The oncogene E6 and p53 expression were analyzed by SYBR Green real-time PCR and western blot. Cell apoptosis was analyzed by flow cytometry.

Results: Andrographolide exhibited cytotoxic effects with IC50 values of 152.34 μM and 142.23 μM, whereas sub-cytotoxic values of 9.71 μM and 13.88 μM in C33A and SiHa cells, respectively. The result demonstrated that sub-cytotoxic concentration of andrographolide suppressed LCR transcription activity of both HPV16 European and Asian variant in transfected-C33A cells. Andrographolide also significantly inhibited E6 oncogene expression in SiHa cells at 24 h post treatment. Importantly, inhibitory effect was increased by increasing concentration, but not time increasing. After 48 h post treatment, the p53 was restored expression in SiHa cells. In addition, andrographolide also significantly induced apoptosis of SiHa cells in concentration-dependent manner.

Conclusion: This result demonstrated that the andrographolide induced SiHa cells apoptosis via suppression of HPV16 transcription activity, leading to decreased E6 oncoprotein and restored p53. These findings imply that the andrographolide may be an effective agent for cervical cancer prevention and treatment.

http://dx.doi.org/10.1016/j.ijid.2012.05.192

Type: Poster Presentation

Final Abstract Number: 40.031
Session: Virology and Viral Infections (Non-HIV)
Date: Thursday, June 14, 2012
Time: 12:45-14:15
Room: Poster & Exhibition Area

Presence of oncogenic viruses (EBV, HHV-6, BKV and JCV) DNA sequences in renal cell carcinoma

A. Farhadi[1,*], A. Behzad-Behbahani[2], B. Geramizadeh[3], Z. Sekawi[1], M.S. Shiran[4], F. Aboualizadeh[2]

[1] *Department of Medical Microbiology and Parasitology, Serdang, Malaysia*
[2] *Diagnostic Laboratory Sciences & Technology Research Center, Shiraz, Iran, Islamic Republic of*
[3] *Transplant Research Center, Shiraz, Iran, Islamic Republic of*
[4] *Department of Pathology, Serdang, Malaysia*

Background: Renal cell carcinoma (RCC) represents five percent of adult epithelial cancers with the annual increase in incidence rates. Smoking, obesity, hypertension and some certain genetic conditions such as von Hippel-Lindau (VHL) disease are partly considered as the risk factors for RCC. However, the possible involvement of oncogenic viral infections as additional risk factors in different subtypes of RCC has not been investigated significantly. Previous studies have found Epstein-Barr virus (EBV), Human herpesvirus 6 (HHV-6) and human polyomaviruses BKV and JCV DNA sequences in kidney tissue and strong data suggest that these viruses possess oncogenic potential in different experimental models. This study was aimed to determine the presence of these viruses in RCC specimens and their surrounding non-tumoral tissue and to examine a possible relation with pathological data.

Methods: A total of 71 formalin-fixed, paraffin-embedded tissue samples from patients with histologically proven RCC and their respective surrounding normal kidney tissue specimens were available for this study. A modified proteinase K/phenol-chloroform protocol was used for isolation of genomic DNA. Nested-PCR assays were employed targeting BamHI, major capsid protein and large T antigen gene regions of EBV, HHV-6 and human polyomaviruses (BKV and JCV) respectively. Further investigation was performed using restriction endonuclease analysis to discriminate the A and B variants of HHV-6.

Results: Of the 71 RCC cases (40 with conventional clear cell, 19 with papillary, 10 with chromophobe, 1 with collecting duct and 1 with unclassified histologic subtypes) EBV, HHV-6 (variant B) and JCV were detected in 31%, 15.5%, and 16.9% of samples, respectively, compared with 4.2%, 9.9%, and 11.3%, respectively, of samples from peritumoural tissue. Only one non-tumoral kidney tissue sample was found to harbour BKV-DNA with a frequency of 1.4% while it was not detected in any of the RCC specimens. Matched-pair analysis indicated that the prevalence of EBV infection among the analyzed cases significantly differ with respect to nontumoral cases ($P = 0.031$). However, such difference was not observed for the other viruses.

Conclusion: EBV was the virus most frequently detected in RCC specimens and viral sequences were significantly present more often in tumors than in normal tissue. These results suggest that EBV may be involved in the pathogenesis of RCC.

http://dx.doi.org/10.1016/j.ijid.2012.05.193